2012 Integrative Healthcare Symposium

Treating the Pain of Lyme Disease and Adopting Lifestyle Change as Therapy

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The Integrative Healthcare Symposium welcomed more than 1,100 practitioners of functional (patient-centered), alternative, and complementary medicine from February 9 to 11, 2012, in New York. This article reviews two key presentations. Richard Horowitz, MD, has treated more than 12,000 patients with chronic Lyme disease. Dean Ornish, MD, was one of the first physicians to scientifically demonstrate that coronary atherosclerosis could be reversed without drugs or surgery.

Pain-Management Strategies In the Chronically Ill Lyme Disease Patient

- Richard Horowitz, MD, Hudson Valley Healing Arts Center, Hyde Park, N.Y., and President of the International Lyme and Associated Diseases Educational Foundation, Bethesda, Md.

Chronic Lyme disease is a symptom complex of borrelial organisms and multiple co-infections with bacteria involving *Borrelia burgdorferi*, *Anaplasma phagocytophilium, Ehrlichia chaffeensis, Babesia*, piroplasms and other parasites, *Bartonella, Mycoplasma*, and *Rickettsia*. Additional sources of infection include other bacteria and viruses that are now widespread in ticks. In the mid-1990s, Krause et al. noted that multiple co-infections may suppress the immune system or may cause a nonspecific stimulation of the immune system, leading to inflammation, pain, and immune dysfunction.[1]

In 2009, Dr. Horowitz suggested that the term multiple chronic infectious disease syndrome (MCIDS) would more precisely describe patients with longstanding borrelial infection and co-infections who are experiencing chronic fatigue, muscle and joint pain, neuropathy, and neuropsychiatric abnormalities. In these patients, he said, multiple overlapping etiologic factors are responsible for their symptoms.

After commenting that his typical patient has already been seen by 15 to 20 specialists, Dr. Horowitz outlined an integrative approach, based on addressing "the 3 I's" (infection, immunity, and inflammation) and on using a differential diagnosis model including evaluation of neurotoxicity; allergies; nutritional and enzyme deficiencies; psychological factors; viruses; and endocrine and gastrointestinal disorders.

First among the remedial steps, treating infection demands a strategy for combatting all three subtypes of *B. burgdorferi* infection, including cell wall, cystic, and intracellular forms.

"If you treat all three forms, you'll generally have much better results than using one drug at a time," Dr. Horowitz commented.

Both acute and chronic pain may be manifestations of chronic Lyme disease and MCIDS. Lyme disease, its co-infections, viruses, and opportunistic infections, such as *Candida*, may be responsible for driving chronic pain syndromes.

"Chronic Lyme disease and MCIDS," Dr. Horowitz said, is the "great imitator.[2–5] Under its commodious umbrella lies a host of pain syndromes, including symptoms of chronic fatigue and fibromyalgia, autoimmune disease, neurological pain (headache, migraine, trigeminal neuralgia, radiculopathy, encephalopathy, cranial nerve palsies, carpal tunnel/ulnar neuropathy), gastrointestinal disorders (irritable bowel syndrome, inflammatory bowel disease), genitourinary disorders (interstitial cystitis), gynecological disorders (dyspareunia, neuralgia), cardiac disorders (costochondritis, pericarditis, palpitations), psychogenic disorders (depression, psychosis, obsessive–compulsive disorder, anxiety-related pain), endocrine disorders (early andropause, irregular menses, low growth hormone levels, pituitary failure), and ophthalmological disorders (conjunctivitis, uveitis, retinitis, optic neuritis).

The infecting agents cause inflammation through various pathways such as interleukin-1 (IL-1), IL-6, tumor necrosis factor–alpha (TNF-α), nitric oxide, and its metabolites, thereby creating free radicals and oxidative stress, which damage cell membranes, mitochondria, and nerve cells. Autoimmunity may also result when antibodies cross-react with tissue antigens. Mitigating these effects requires multiple strategies, including:

- treating infection, immunity, and inflammation (the 3 I's).
- supporting detoxification pathways in the liver, skin, kidneys, and lymph system.
- balancing hormones.
- addressing nutritional deficiencies, food allergies, and sleep disorders.
- eliminating environmental triggers, such as heavy metals (a further source of inflammation).

Dr. Horowitz summarized the pain-relieving strategies that he developed while treating more than 12,000 patients with Lyme disease with overlapping chronic fatigue and fibromyalgia syndromes.

"It is the cytokines that are really driving the pain," he said.

In attempts to identify the source of the patient's pain, a multifaceted approach with the 15-point model works best.

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"Usually, the sickest patients require a combined approach using pharmaceuticals and nutraceuticals," he added.

Referring to some classical treatment recommendations, Dr. Horowitz said that nonsteroidal anti-inflammatory drugs (NSAIDs) might be effective for muscle and neuropathic pain. Antidepressants that block norepinephrine uptake are usually more effective than those that inhibit serotonin. Combinations of tricyclic antidepressants and gabapentin (Neurontin, Pfizer), with or without opioids, improve analgesia at lower doses compared with single analgesics alone. Intravenous (IV) immunoglobulin is the treatment of choice for small-fiber neuropathy. Minimally invasive, often successful techniques for refractory pain include electronic stimulators, pulsed radiofrequency, and botulinum toxin A.

As for integrative pain therapies, Dr. Horowitz said that low-dose naltrexone (ReVia, Duramed) has proved effective in Crohn's disease, multiple sclerosis, and fibromyalgia. In his open-label study of 500 patients with Lyme disease and MCIDS, approximately 75% of patients experienced less fatigue, myalgia, and arthralgia when the naltrexone dose was titrated to 4.5 mg at bedtime.

For the patient with a stimulated immune system that produces inflammatory cytokines, alpha-lipoic acid (ALA), glutathione, the phenol resveratrol, and curcumin have been found to relieve pain, fatigue, and "brain fog." When cytokine levels are too high, IV or oral glutathione—a therapy that is often underused—is very safe. Compounding pharmacies, Dr. Horowitz offered, could combine resveratrol, curcumin, and ALA to decrease cytokine levels. To avoid systemic effects in patients needing therapy for localized pain, he suggested that dimethyl sulfoxide (DMSO), along with these agents and others (e.g., low-dose naltrexone, glutathione, and anti-inflammatories) could be absorbed into creams.

Angiotensin-receptor blockers (ARBs) reduce TNF-α levels and may be useful for persistent inflammation, especially if the inflammation is associated with uncontrolled hypertension.

Anti-inflammatory foods, such as those in the Mediterranean diet (fruits, vegetables, fish, and whole grains), or very-low-carbohydrate diets with small, frequent meals may be helpful in reducing inflammatory responses for patients with metabolic syndrome and insulin resistance.

The herbs *Andrographis paniculata, Polygonum cuspidatum* (resveratrol extract), *Stephania tetranda* root, and *Smilax rotundifolia* (common greenbriar) all have strong scientific backing in patients with ongoing symptoms and inflammation, Dr. Horowitz said.

Nuclear factor (erythroid-derived 2)-like 2 induces the expression of genes for several antioxidant enzymes and may help to regulate oxidative stress. Because acute and chronic episodes of psychological stress can induce inflammatory processes,[6] stress reduction through meditation, yoga, or *Tai Chi* is also recommended.

Dr. Horowitz concluded that treating the three forms of *B. burgdorferi*, co-infections, hormonal abnormalities, heavy metals, neurotoxins, sleep disorders, psychiatric problems, and nutritional deficiencies is the best way for patients to regain their health and to decrease pain.

"Most conventional practitioners don't believe that Lyme disease exists in chronic form, because they think the blood tests are reliable when they come up negative. But ELISA [enzyme-linked immunosorbent assay] is unreliable; you need a Western blot looking at the Lyme-specific bands from a good lab," Dr. Horowitz said.

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The Power of Lifestyle Change and Love

- Dean Ornish, Clinical Professor of Medicine, University of California, San Francisco

Dr. Ornish has been a pioneer in promoting the idea that lifestyle change is a form of active treatment, not just a disease-prevention measure, since his ground-breaking research first showed that a combination of diet, exercise, meditation, and psychosocial support could reverse the progression of atherosclerosis and the incidence of cardiac events.[1] Subsequent research has extended the evidence for those benefits to include reducing prostate-specific antigen (PSA) levels, down-regulating oncogenes that promote breast and prostate cancer,[2] and decreasing the incidence of prostate cancer itself.[3]

Initial responses to Dr. Ornish's program for lifestyle change have often included begrudging acknowledgment of its effectiveness, accompanied by the objection that few patients would be able to accept and withstand the rigors proposed in his regimens. Posing the question, "What enables people to make sustainable changes in their lives?", Dr. Ornish cited an analysis of more than 37,000 patients who were new to statin drugs such as atorvastatin (Lipitor, Pfizer), fluvastatin (Lescol, Novartis), lovastatin (Mevacor, Merck), pravastatin (Pravachol, Bristol-Myers Squibb), and simvastatin (Zocor, Merck). After a year, only 18% to 38% continued with therapy.[4]

"Fear is not a sustainable motivator," he said, adding "nor is information sufficient to motivate most people to make sustainable lifestyle changes." The solution, in part, according to Dr. Ornish, is for health care practitioners to "… reclaim our role as healers, not just as technicians."

To provide the kind of personalized medicine implicit in such a philosophy, Dr. Ornish has striven pragmatically toward what he termed a "radical simplicity," suggesting that patients choose to what degree and at what speed they take up lifestyle change. Rather than brandishing fear-based risk-factor modification, he advocates the combination of "fun, freedom, pleasure, and love" as a means toward feeling better, living longer, losing weight and gaining health.

In terms of replacing drugs with lifestyle change, the program is hardly absolutist. In an interview, Dr. Ornish said:

"The synergy for combining lifestyle change with drugs is optimal for many patients. For example, the chances of them sustaining their adherence to statin drugs is much higher if they change their lifestyle, and the drugs work better, as well—that's true not just with statins, but with drugs for other chronic conditions such as hypertension and obesity."

Among the patients in his program who are taking statins, adherence rates range from 85% to 95%, just as they are for the program's comprehensive lifestyle changes and other medications.

"When patients feel that they are active participants, not just passive victims, they are empowered and become more compliant with medication regimens in general," he said.

Another pragmatic shift in to Dr. Ornish's work was based on the realization, "If it's not reimbursable, it's not sustainable."

Sixteen years of effort were fulfilled on January 1, 2011, when Medicare Part B began covering the Medicare Lifestyle Demonstration Project, a comprehensive effort for reversing the effects of arteriosclerosis. That decision was based, in part, on a demonstration project during which Highmark Blue Cross Blue Shield compared patients who participated in the Ornish program with a similar group of patients who were not enrolled. Overall health care costs in the program's patients declined by 50% after only 1 year and by an additional 20% to 30%, compared with a matched control group. In the earlier Multicenter Lifestyle Demonstration Project, nearly 80% of 333 patients who were eligible for bypass surgery or angioplasty were able to safely avoid invasive procedures by changing their lifestyle through diet, stress reduction, and exercise.[5,6] The January 2011 decision was the first time Medicare had covered an integrative medicine program.

"Now that we've shown that it is both clinically [effective] and cost-effective, it should be easier for others. Reimbursement is what makes this feasible and sustainable," said Dr. Ornish.

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